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To promote good nutrition and informed use of drugs, food, medical devices and natural health products, and to maximize the safety and efficacy of drugs, food, natural health products, medical devices, biologics and related biotechnology products in the Canadian marketplace and health system.

Health Products and Food Branch Inspectorate

Summary Report: Stakeholder Consultations on the Good Manufacturing Practices (GMP) Inspection Program Review

Date issued:
January 26, 2011

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1.0 Introduction

Health Canada is currently conducting a review of its Good Manufacturing Practices (GMP) inspection program for drug establishments in an effort to make the program more risk-based. Further to this review, Health Canada undertook face-to-face and on-line stakeholder consultations during the fall of 2009. This report provides a summary of the feedback that was received on-line and during face-to-face sessions.

2.0 Consultations

2.1 On-line consultations

The on-line consultation workbook (<http://www.hc-sc.gc.ca/dhp-mps/consultation/compli-conform/2009gmp-bpf-book-cahier-eng.php>) was available through the Health Canada website from September 15 through to November 30, 2009. All drug establishment licence (DEL) holders and industry associations received an electronic notice, informing them of the workbook and inviting them to participate.

The on-line consultation workbook asked for input on three key concepts: (i) how to best assess the risk posed by an establishment's activities; (ii) appropriate inspection cycles for different levels of risk; and (iii) tools that can be developed to make the inspection program more risk focused.

The Health Products and Food Branch Inspectorate was pleased with the on-line participation and received a total of 80 submissions. A significant number of stakeholders reported difficulty in using the Health Canada website to complete the on-line consultation workbook; in such cases, an electronic version of the consultation workbook was sent and returned via email.

2.2 Face-to-face consultations

The same notice that informed stakeholders of the on-line consultation workbook, also invited people to register for one of 6 face-to-face sessions (<http://www.hc-sc.gc.ca/dhp-mps/consultation/compli-conform/2009gmp-bpf-index-eng.php#workbook>). Sessions were held in Vancouver, Edmonton, Winnipeg, Toronto, Ottawa and Montreal and a total of 255 stakeholders participated.

Stakeholders reacted very positively to having the opportunity to meet face-to-face with Health Canada personnel, outside of establishment inspections. The consultations were well-attended and stakeholders participated fully, both in plenary and breakout sessions. Most participants liked the breakout group format and seized the opportunity to interact with other members of their professional community and other sectors of their industry.

Constructive feedback was received in all cities that Health Canada visited. As enrolment could have been higher, Health Canada was encouraged to try additional methods of promotion and to improve the ease of use of the Health Canada website. Many participants voiced that the consultations were too focussed on fabricators, rather than having an even distribution of focus for all sectors of industry.

3.0 Major Topics discussed during the Consultations

This report deals with the major topics that were discussed during the consultations:

- Proposed Risk Criteria
- Risk Level and Inspection Cycle for different Companies
- Developing New Tools – Compliance Report
- Developing New Tools – Abbreviated Inspections
- Questions and Answers

The topics that were explored during the online and face-to-face consultations were similar, but not identical; therefore participants from one or the other consultation forum may see new material covered. (A list of additional questions asked by participants can be found in Appendix A.)

3.1 Proposed Risk Criteria

Participants were asked to discuss the criteria that they believed should be considered when determining the risk level of an establishment. (See Appendix B for the list of criteria that was provided for discussion, with a short description of each.)

Stakeholders were provided with eleven risk criteria and were asked to discuss them and categorize them into two groups: those they considered most important and those they considered less important. Many stakeholders created criteria groupings (e.g., 3 criteria together) that they considered to be intrinsically related. Still others developed various matrices, grids and weighting scales to deal with the relative importance of the criteria.

In addition to identifying top five risk criteria and bottom five risk criteria, on-line participants were asked to provide reasons for supporting and not supporting risk factors. These valuable comments form the basis for the discussion below.

The following are the criteria that received the most support:

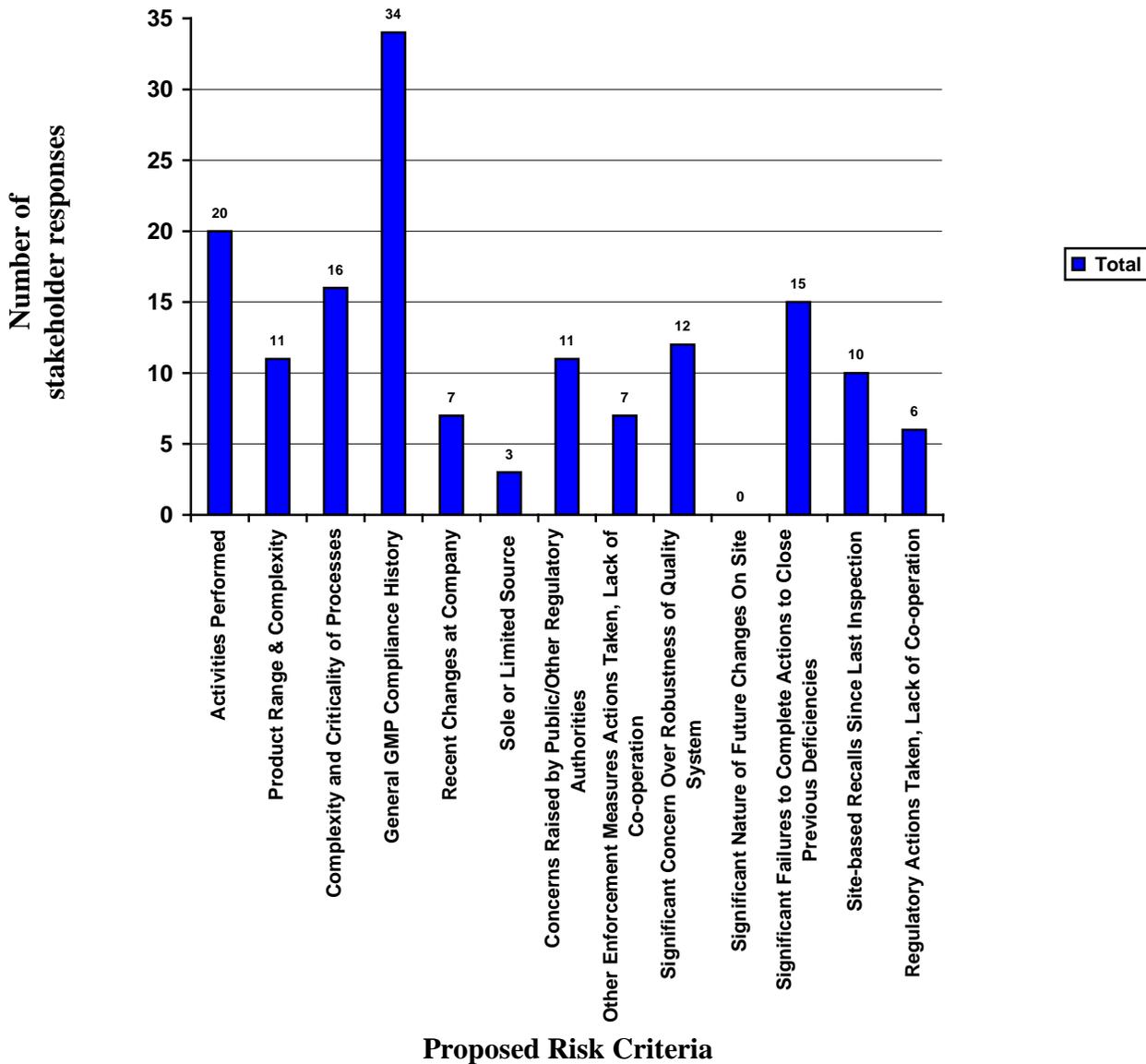
- Complexity and criticality of processes
- General Good Manufacturing Practices (GMP) compliance history
- Significant concern over robustness of quality system
- Significant failures to complete actions to close previous deficiencies
- Activities performed

The following are the criteria that received the least support:

- Sole or limited source
- Recent changes at company
- Concerns raised by public/other regulatory authorities
- Other enforcement measures/regulatory actions taken, lack of co-operation
- Site-based recalls since last inspection

Another criterion, *product range and complexity*, fell in the middle, with almost equal top and bottom votes. (The risk factor *significant nature of future changes on site* was used on-line but was not included in the face-to-face consultative process.)

Figure 1.0 Support for various proposed risk criteria



Virtually all participants agreed that *GMP compliance history* is a very important risk factor. One stated that historical compliance data demonstrates a consistent control level, predicts continuing GMP compliance and reveals the credibility of an establishment. It was recommended that compliant Drug Establishment Licence holders with low risk observations be recognized by having less frequent inspections. Others suggested that Health Canada should not only consider the number of past observations, but the corrective actions taken and any follow-up inspection that was required. Health Canada was given caution that this factor is easily applied

when there is a prolonged negative compliance rating; however, this requires fairness to differentiate between recommendations and low risk observations versus genuinely substantive observations.

Stakeholders strongly supported the risk factor *complexity and criticality of processes*, and the reason was most succinctly explained by one participant as ‘complexity is inherently riskier than simplicity’. It was also said that complex and more robust processes are usually used for high-risk products, such as biological, sterile, or delayed-release drugs. For newly-approved products, it was recommended that inspection focus on the ability to consistently manufacture relative to the clinical batch and assess the critical process parameters, including the application of Quality by Design.

With respect to the criteria *activities performed*, several participants stated that risks associated with fabricating, testing, packaging, and labelling (activities that have a primary impact on quality) are higher than with importation/distribution or wholesaling (activities which review documentation and manage storage and transport). Other participants explained that (i) certain activities are inherently associated with higher risk in terms of the efficacy, safety, and stability of a product, (ii) activities that are more complex mean more controls and thus more risk, and, (iii) all activities should be able to be considered low risk if they are consistently compliant.

Significant failures to complete actions to close previous deficiencies also received support. One participant stated that Establishment Licence holders must be accountable to address all observations following each inspection, whereas another countered this by saying that this risk criterion should only apply to risk 1 observations. Some stakeholders supported this risk factor because they thought that such failures show a failure of the quality system, and that previous deficiencies that have not been properly addressed can greatly impact the safety and quality of the product.

Succinct comments that were received pertaining to the risk factor *significant concern over robustness of quality system* were that a quality system is critical to product quality and that a quality system that is not robust allows errors to go unnoticed. It was mentioned that this risk item provides a very good measure of management commitment.

Although some participants did promote that sole source establishments should be monitored well, with due consideration given to their compliance, *sole or limited source of supply* received little support as a risk criterion. It was mentioned several times that this criterion boils down to a supply issue or a commercial risk, not a safety issue. Another argument against including it as a risk factor was that this would imply that companies who have a product that is first-in-class would have a higher risk profile.

There was not a great deal of support for *recent changes at company* as a risk factor. One participant pointed out that the relevance of a particular change would depend on its degree, importance and impact, so perhaps a major or significant change would have to be defined. Other reasoning included that changes should not be an issue for companies with a good compliance history and, similarly, that a good quality system should be robust enough to handle change.

The risk criterion of *Concerns raised by public/other regulatory authorities* appears to have diminished support based on the public being included in the criterion. It was said that the public, in general, lacks sufficient technical knowledge about GMP and that concerns tend to be subjective. Participants were more supportive of taking into consideration concerns that are raised by other regulatory authorities. One advisement that was received was that every concern requires evaluation on a case-by-case basis.

The risk factor *other enforcement measures/regulatory actions taken, lack of co-operation* garnered mixed reaction from participants. Some found that the combined factor was not clear enough, so they could not provide clear feedback on it. Others said that this was a compliance and vigilance issue and thus did not belong in the GMP arena. One participant pointed out that co-operation from industry is voluntary, but that does not mean that it is automatically given.

With respect to *site-based recalls since last inspection*, multiple participants pointed out that a recall can actually show compliance with regulations, indicate a robust quality system, and may not reflect the GMP compliance status, depending on the cause. Another said that multiple site-based recalls raise issues of credibility and can be an indicator of poor quality management. Other comments included that the factor would be relevant if the site-based recall demonstrates that there is a lack of control of GMP, or if a major trend is observed. It was suggested that recalls could be incorporated into *GMP compliance history* and that Health Canada's assessment should relate to the effective control of the recall activity and the implemented corrective actions. Health Canada was asked to consider the seriousness, transparency and efficiency of the recall. It was suggested that recalls as a risk should exclude those due to adverse effects or medical efficacy.

As mentioned above, *product range and complexity* fell squarely in the middle between the top and bottom 5 when all consultation totals were taken into consideration. Those who support it as a risk factor say that the chance of error increases with an increase in the number and the complexity of products produced. Those who are not in support of it say that the number of products should not be an issue if the company is GMP compliant and that company experience is a better indicator of risk. Aligned with this thinking is another submission that yes, there is a spectrum of risk associated with product complexity, but it is more important that proper compliance controls are in place.

3.1.1 Missing Risk Criteria

Health Canada asked if we had missed any risk criteria. The following are some of the ideas that were suggested:

- Country of origin for both ingredients and final product
- Number of foreign sites on Drug Establishment Licence (DEL)
- Multinational versus Canadian only company
- Newly-established products, technologies or systems (e.g., making a dosage form for the first time or using cold chain management for the first time)
- Volume of products on market, measured in doses, not dollars (e.g., acetaminophen is available everywhere)
- Corporate compliance history (Good Manufacturing Practices history is site specific)
- Evidence of fraud
- Toxicity of by-products and potential contaminants
- New company, without a manufacturing or compliance history
- Types of subcontracting activities carried on by a company and their complexity
- Other regulatory approvals already received
- Actions taken with respect to the company by other divisions within Health Canada and/or regulatory action taken against another division of the same company
- Personnel considerations, including turnover at management level and that advantage should be given to companies with adequate number of qualified, well-trained personnel
- Emergency situations (e.g., fire or computer system crash)

3.1.2 Special Considerations

Health Canada asked in-person consultation participants if there were any special considerations that should be taken into account when determining risk, depending on the establishment’s type(s) of activity. The following are some examples of the feedback received:

- No, this is included under the risk criterion *Activities performed*
- Yes, there are special considerations, however this depends on case-by-case evaluations (e.g., human versus veterinary drugs, parenteral versus oral versus topical drugs, over-the-counter versus prescription drugs, sterile versus non-sterile drugs)
- For fabricators, if toxic and non-toxic products being produced at the same site
- Importers have special considerations with respect to countries of origin and how many sites the importer is importing from
- Recalls should not apply to importers, instead action should be taken with the foreign fabricator
- Cold chain management for wholesalers
- For packagers, primary versus secondary packagers
- Third party logistics warehouses and their customers

3.2 Risk Level and Inspection Cycle

Stakeholders were also asked what they thought an appropriate inspection cycle is for higher, medium and lower risk establishments, respectively, and for any explanations.

Figure 2.0 Support for various proposed inspection cycles for high risk establishments

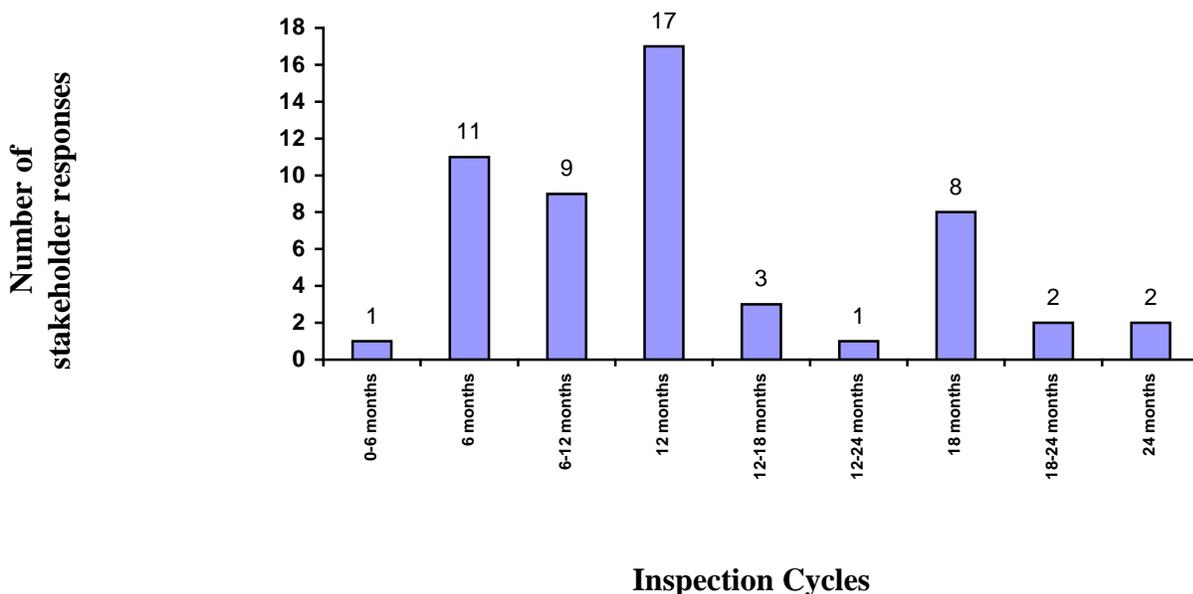


Figure 3.0 Support for various proposed inspection cycles for medium risk establishments

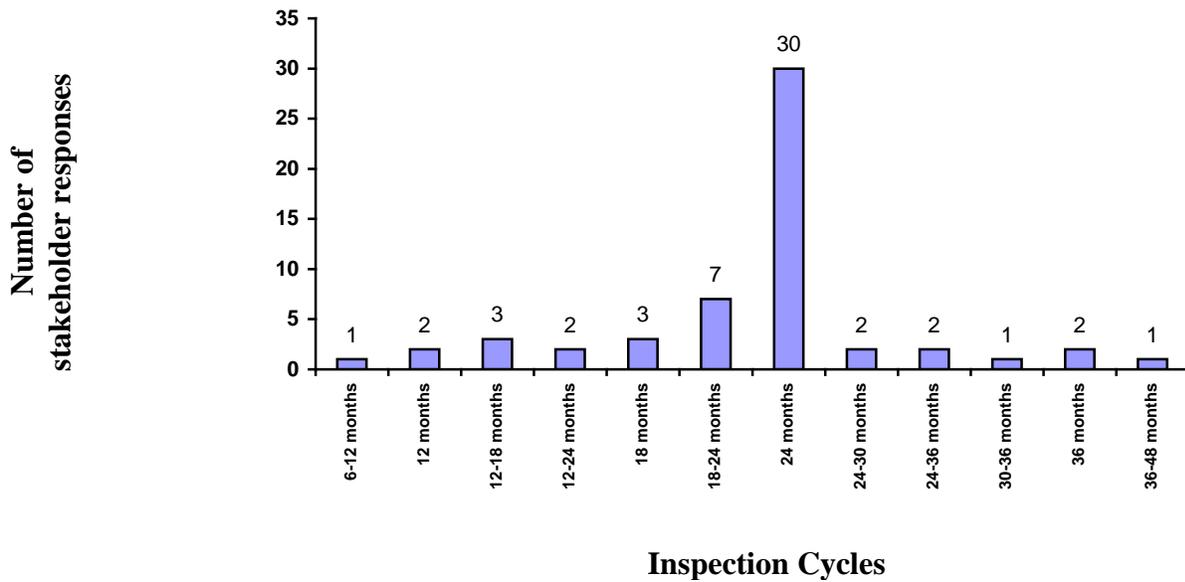
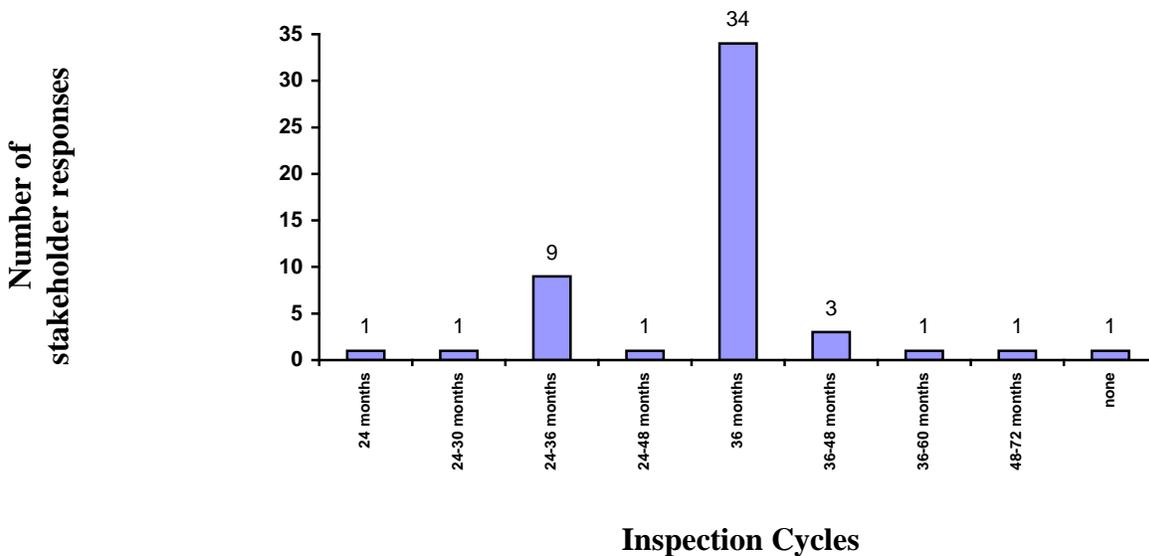


Figure 4.0 Support for various proposed inspection cycles for low risk establishments



In the face-to-face consultations, break-out groups were also asked to analyze mock inspection reports for three different companies, and then assign each company (i) a site risk level of High, Medium or Low and (ii) a corresponding risk-appropriate inspection cycle. This exercise really captured the participants' interest and while nothing was unanimous, definite trends emerged.

The results are found below. The suggestions regarding inspection cycle are very well-aligned with the on-line submissions. On average, stakeholders agreed that a higher risk establishment should be inspected every 12 months, a medium risk establishment every 24 months and a lower risk establishment every 36 months.

Chart 1.0 Results of break-out group exercise when analyzing mock inspection reports for three different companies to determine site risk level and corresponding risk-appropriate inspection cycle

	Company A	Company B	Company C
Description	Sterile Manufacturer, Tester and Distributor of Parenteral pharmaceuticals and vaccines	Non-sterile Fabricator, Packager, Tester and Distributor of Medical Gases	Non-sterile Fabricator, Packager and Tester of Oral Dosage Forms
Risk Level	High (clear result)	Low-Medium	Medium (clear result)
Appropriate Inspection Cycle	12 months (clear result)	24-36 months	24 months (clear result)

The following are some of the additional comments that were received from participants:

- Need a clearer definition of high, medium, and low risk and requested a better understanding of the weighting of all risk factors
- Not a good idea to extend inspection cycle and do abbreviated inspections (explained below) for same company
- Extension of inspection frequency should be granted as an earned privilege, not a right, for being compliant
- Documentation issues are not as critical as actual product or process failure
- Cycle length of 6 months may not be feasible, resource-wise, for multinational companies that are inspected by many regulatory agencies
- Must consider the practicality of a 6-month inspection, suggesting a 12-18 month cycle is required in order to provide sufficient time to demonstrate on-going, sustainable improvement.
- Companies may plan budgets and resources based on the current 2-3 year inspection cycles and any changes to cycles should not be too disruptive to businesses
- Health Canada should be transparent with companies about cycle assignment and reasoning
- Manner in which observations are written provides context which will be important if they are later used to assess the risk and frequency of inspection
- For multi-Drug Establishment Licence (DEL) site companies an inspection deficiency is usually corrected across all sites - recommend rotating each site within a company every two years
- Adopt a United States Food and Drug Administration approach for low risk establishments (especially veterinary products)

3.3 Developing New Tools

3.3.1 Compliance Report

The Health Products and Food Branch Inspectorate is considering using a Compliance Report in order to gather information in advance of an on-site inspection, with the goal of facilitating a more informed and

streamlined inspection. A Compliance Report would include a summary of changes in site performance or activities since the last inspection, such as changes in any of the following areas: key personnel or staff numbers, company ownership, structure or status, processes or products and facilities or equipment.

The feedback received on the Compliance Report was extensive. General comments included the desire to see a Compliance Report focus on fostering collaboration from establishments, rather than the Report being seen as a burden to industry. If the Report simply functions as a pre-inspection checklist and the inspection is going to happen anyway, some did not see any potential value. Health Canada was also encouraged to ask for this information on an annual, or even more frequent, basis, rather than only prior to an on-site inspection. Changes, whether positive, negative, or neutral, could potentially be submitted electronically and on a fairly on-going basis.

Strong commentary surrounded the clarity and language of the draft Compliance Report provided its benefit to industry and overall value. On a general level, some questioned what the purpose of the Report would be, realizing it is for information-gathering, but then asked what will be done with all of the information? There was a request for far more clarity with reference to what information is actually desired in response to the questions.

What did participants like about the proposed Compliance Report?

There was consensus that a tool like the Compliance Report would facilitate better planning and preparation for inspections by both Health Canada and establishments. It was thought that having timely and accurate information in advance would be invaluable and that such a report could help with inspector focus and could provide guidance as to what an establishment should expect during an inspection.

Establishments were supportive of a Compliance Report that would provide the possibility of less frequent and/or shorter inspections. If a tool could decrease the overall time and resources involved in the inspection process then it would be enthusiastically received. Participants said that it has to be made clear to companies that if they co-operate with the submission of a document like this then things will go more smoothly for their time and resource allocation. Otherwise, without time savings, the overall value of the document was frequently questioned.

In sum, participants thought that a Compliance Report is a great idea, in concept, that it communicates important changes and that it has the potential to benefit both Health Canada and establishments. Some companies noted that a Report could easily be completed by industry based on routine information that the company already has available. It is also thought a reporting tool like this could foster better communication between Health Canada and Drug Establishment Licence holders.

What did participants dislike about the proposed Compliance Report?

Stakeholders were most concerned with a few common issues. First, the Health Products and Food Branch Inspectorate received numerous comments about the content and format of the sample Compliance Report, as it was provided. It was thought that the Report asked for information that is far too general in nature. It was suggested that Health Canada should require more specific categories in order to encourage complete, consistent and useful reports among companies and sites. In addition to clarity, more precise guidance with respect to how to fill out the form, and what to include and at what level of detail, was requested. The inclusion of simply-formatted, user-friendly checklists was encouraged, in order to generate user participation and also clear answers which are less subject to interpretation. If similar information will be asked for year after year then participants thought registering only necessary changes should be an option.

Many participants focussed on the section of the Report that requests information on changes. The use of the phrase “significant change” was thought to be too subjective and the relevance and/or benefit of knowing about key personnel or staff number changes was called into question. It was suggested that the Health Products and Food Branch Inspectorate should describe what is meant by “changes” and define “key personnel,” among other things. Without clear direction, there is the chance that the Health Products and Food Branch Inspectorate could get bombarded with extraneous information that was never actually wanted, perhaps resulting in more questions than answers.

It was noted that the Compliance Report, as proposed, was too fabricator-oriented and did not necessarily apply as well for importers, distributors and wholesalers. Along with calls for a more specific questionnaire, mentioned above, some stakeholders suggested questionnaires that are tailored to industry type.

The issue of the timing of the submission of the Report was also mentioned several times during consultations. The sample Compliance Report that was put forth at the consultations included the statement that “[...] and return to your inspector’s email address no less than one month prior to your inspection.” Submission one month before an inspection was generally thought to not be long enough before the inspection. This length of delay was considered too short to implement any necessary change in inspection cycle. Considering this, some questioned the objective of the Report in assessing risk in order to determine an inspection cycle. Many participants proposed that the Report be submitted as an annual report, perhaps sent in conjunction with a Drug Establishment Licence (DEL) renewal.

Stakeholders addressed the manner of submission of a Compliance Report. The Health Products and Food Branch Inspectorate example, as given, asked that the form be completed electronically and returned by email. It was pointed out that companies consider some of this information to be confidential and that it thus should not be sent by email. Some DEL holders said that they would prefer a secure, web-based technology that would allow them to log on in real time and update their information, whenever they have changes, not just annually. Others pointed out that they do not think that electronic submission of any sort is confidential and they do not want their confidential information to be put in jeopardy at any time, especially by Access to Information Requests. Some added that it is better to address confidential or complex issues during an on-site inspection.

Attention was drawn to the signature requirements at the end of the Compliance Report. Opinions were divided on the inclusion of executive signatures. Some saw it as of no value whatsoever while others thought it was very good to have their executives accountable for something of this nature. Substitute signatures, like those of any senior officer or a consultant, or the person responsible for the site, were also suggested. For example, some companies might not have Chief Executive Officers (CEOs) or CEOs might be located off-site. In addition, some argue that a high level officer may not have the requisite knowledge to provide an attesting signature.

Finally, what the Health Products and Food Branch Inspectorate staff heard repeatedly was that Health Canada needs to establish better internal communication among its Directorates. The request for most of the information on the Compliance Report was called “redundant” and of little added value because DEL holders asserted that most of the information that is requested is already known by Health Canada and should be on file. Participants expressed that this request for the same information was a burden for industry. Companies would prefer to help Health Canada gather other information that has not already been provided to HC or information that is perhaps more precise than what is on file.

Are there other ways in which the Health Products and Food Branch Inspectorate could obtain the necessary, up-to-date information?

The resounding answer to this question was that Health Canada should look internally for this information. Participants said that most of the information being requested on the sample Compliance Report was already known by Health Canada, through previous submissions to various parts of the department. Examples given included Site Reference Files, Annual Product Quality Reviews and the DEL application, among others. It was suggested that Health Canada first use internal information and then, for that information which is not available, ask for further information directly from companies.

Some stakeholders were also willing to submit new information or updated information on-line. They indicated that they would appreciate being able to access their last submission in order to provide a response and indicate if there have been any changes. Combining the ideas of Health Canada having better internal communication and the willingness to submit information on-line, it was suggested that Health Canada have a single repository of information, or a “master file,” into which companies could submit their information.

Other suggested methods of gathering information were reading a company’s website, placing pre-inspection telephone calls and accessing other regulatory authorities’ inspection reports. It was also mentioned that new companies could be provided with a checklist in advance of their first inspection so that they know what to expect.

3.3.2 Abbreviated Inspections

Stakeholders who participated in the face-to-face consultations were given a description of potential abbreviated inspection model tools. Abbreviated inspection tools are being considered for inclusion in the national toolkit for the Health Products and Food Branch Inspectorate. Such inspections could be offered to selected establishments, based on the establishment’s overall compliance history. Abbreviated inspections are potentially shorter in duration, perhaps less in-depth, with a focus on quality systems. Abbreviated inspections would entail the inspection of an establishment’s quality system during each and every inspection.

Feedback was requested on the Pros and Cons of abbreviated inspections and ideas were requested on whether abbreviated inspections would be more suitable for establishments engaging in a certain type of activity.

Stakeholders’ Potential Pros of Abbreviated Inspections

- Would save time and resources, for both establishments and the Health Products and Food Branch Inspectorate. Time savings would primarily be gained through shortening the duration of inspection time on-site.
- Time could also be economized if company knows an abbreviated inspection is coming and know in advance that inspectors will be looking at particular systems or items. This would help a company to reduce preparation time and help them to plan.
- Management acceptance of abbreviated inspections would be more likely if inspectors were to spend half as much time on-site than they customarily have. Also, as industry management comes to understand the value of shortened inspections they may see them as a reward for good compliance and adjust their compliance accordingly in order to spend less overall time in audit mode.

- It would be possible that multiple sites of one corporate entity could be inspected for different aspects that would show the compliance standard of the entire company.
- Would be more cost-effective for businesses that have little change from year to year.
- Have the potential to eliminate distractions and be less diluted by less significant issues and they may permit efforts to be concentrated on legitimate issues that matter to everyone. They could allow for a more thorough examination of issues and their true root cause and could provide an opportunity to focus on high risk items.
- Could provide a deeper or more precise assessment of quality systems, and would make the discovery of quality issues more likely.

Stakeholders' Potential Cons of Abbreviated Inspections

- Something important could be missed if a system is not inspected for an unreasonable amount of time, six years, for example. Such a gap could result in potentially major issues falling between the cracks, not getting noticed for a long time, or being neglected by a company.
- Rewarding good companies could backfire if they become complacent as a result or if they start to favour areas that they know are coming up for inspection.
- It is good for the Health Products and Food Branch Inspectorate to have a general overall view of an establishment and the Health Products and Food Branch Inspectorate could be exposing itself to more risk, considering potential gaps over time.
- It is difficult to clearly separate core systems as there is a lot of overlap.
- Interacting with Health Canada represents a good learning opportunity. If long intervals occur between inspections there would be less valuable information transfer from Health Canada to companies.
- Although the on-site inspection might be shorter, would abbreviated inspections really diminish the workload for everyone involved? Time allotments for preparation and for corrective action follow-up would still be necessary. Some even thought that abbreviated inspections would require more preparation, than occurs now, for both Health Canada and establishments.
- What if there were to be a recurrence of observations in one area? For example, if a company were weak in something and they dealt with it, and then were re-inspected on the same issue a few times, then time is being lost for the inspection of other items. In addition, if a company itself focuses too much on improving one area, it could be detrimental, in terms of decreased compliance elsewhere, as well.
- Such inspections could be overly-detailed in one, or only a few, areas. They could also be too repetitive and carry too narrow a focus.
- These inspections would make consistency in inspections, by different inspectors, a challenge.

Would abbreviated inspections be more suitable for establishments engaging in a certain type of activity (e.g., manufacturing, wholesaling, importing)?

Overall there was not great consensus with respect to this question. Some participants did say that abbreviated inspections might be best suited to companies who conduct several activities (i.e., packaging, fabricating, etc.).

There was agreement that abbreviated inspections are not appropriate for high risk establishments. It was said that a list of risk factor criteria needs to be decided upon, before abbreviated inspections are implemented. For example, based on a risk criteria model, Health Canada perhaps should not allow an abbreviated inspection based solely on the fact that a company has excellent compliance, when they are a vaccine manufacturer.

Participants also put forth that there could be scales of less scope of inspections and less frequency of inspections to reward companies with a good compliance history who are also at low risk. Solidly good companies should be able to work their way towards shorter and less frequent inspections, as a combination product.

Possible patterns for abbreviated inspections were mentioned (e.g., full then abbreviated, then full, etc.), so compliant companies do not become less compliant with time. Regardless, it was expressed that an establishment should always be prepared for a full inspection with their time and resources, and it is a bonus if the inspector decides to do an abbreviated inspection.

4.0 Conclusion

The stakeholder consultations on the Good Manufacturing Practices (GMP) inspection program review provided an effective way to introduce industry to the review and the issues that it presents. Through enthusiastic stakeholder participation Health Canada was able to gather excellent input on risk factors, inspection cycles and new inspection tools.

The consultations are an important and valuable step in the GMP inspection program review and Health Canada's Health Products and Food Branch's Inspectorate is grateful to everyone who participated.

Appendix A – Questions and Answers

Health Canada received many questions during the consultations. Please find below a record of pertinent questions and their answers.

Q1: For Good Manufacturing Practices (GMP) Review matters, is there a requirement to make a regulatory amendment?

A1: Most of our issues would not require a regulatory amendment but if one or more would require a regulatory amendment then we are not dismissing it on that basis.

Q2: Does the (Good Manufacturing Practices Review) framework include changes to Division 1A?

A2: These are separate processes. The Drug Establishment Licence (DEL) expiry on a yearly basis required by Division 1A of the *Food and Drug Regulations* is an administrative burden. There is a separate review of Division 1A underway.

Q3: Do we address foreign inspections?

A3: We realize that we need a foreign inspection program but our current program is domestic and thus this Good Manufacturing Practices (GMP) Review can only be domestic.

Q4: What about products from other countries? What about ensuring products from outside Canada are as safe as those within Canada? If Health Canada's mandate is only to look at domestic inspections and there is an increase in international sourcing, how can Canadians have confidence in goods made in Mississauga as well as elsewhere?

A4: For domestic inspections Health Canada has a set, established program in Canada. For foreign sites things are not as established. The foreign situation is being looked at, but not under the Good Manufacturing Practices (GMP) Review. For foreign sites we rely heavily on our international agreements with our partners.

Q5: Does the Mutual Recognition Agreement (MRA) with Australia include veterinary drugs?

A5: No, and not Natural Health Products (NHPs) either.

Q6: Are wholesalers subject to a 3 year maximum inspection cycle? Do our international agreements have constraints for inspection cycles?

A6: Our international agreements say that inspections for fabricators, packager/labellers, and testers need to be every 2 years. However, wholesalers, distributors and importers are not held to that outer limit. They need to be inspected every 3 years.

Q7: How does this Good Manufacturing Practices (GMP) Review relate to the Cost Recovery Initiative? Could some of the changes recommended as part of the GMP Review mean changes in Cost Recovery? Are the timelines for the GMP Review and Cost Recovery aligned?

A7: If, because of Cost Recovery, changes in how we inspect certain sectors are recommended, then we could include those changes in this project. We did review the minutes from Cost Recovery panels to understand what the issues are. Cost Recovery is interested in what the GMP Review is doing, especially Medical Gases.

Q8: Are there initial inspections prior to the grant of a Drug Establishment Licence (DEL)?

A8: An initial inspection is required for a first time applicant.

- Q9:** What is the timeframe from Drug Establishment Licence (DEL) application to inspection?
A9: If you submit today then Health Canada has 30 days to process the application and then the inspection date has to be set within 60 days. Therefore the inspection generally takes place 90 days from the date a company applies for a DEL.
- Q10:** How many Drug Establishment Licences (DELs) do you issue per year?
A10: Health Canada issues 1100 DELs per year and they are all annual licences.
- Q11:** Is it a possibility that we could not have expiry dates on Drug Establishment Licences (DELs)? (This question is pursuant to a Health Canada slide that says Health Canada is looking at inspection-licensing link.)
A11: Yes, that is a possibility. Annual expiry dates are an administrative burden. The DEL would still carry an annual fee and the DEL could still be used as an enforcement tool (cancellation, suspension, etc.). There are other jurisdictions that do not have expiry dates.
- Q12:** With reference to the new “Good Manufacturing Practices Guidelines, 2009 Edition (GUI-0001)” (<http://www.hc-sc.gc.ca/dhp-mps/compli-conform/gmp-bpf/docs/gui-0001-eng.php>), effective November 8, 2009, should we **not** use this on-line consultation workbook?
A12: The Good Manufacturing Practices (GMP) Review and the new guidelines are not related. The guidelines are technical. The GMP Review is looking at *how* we do the inspections (i.e., the process).
- Q13:** Can you give some examples of *increased complexity* in inspections?
A13: It could be the actual complexity of the processes, and, also, some companies deal with both drugs and medical devices. This could also mean complexity with respect to a product like radiopharmaceuticals.
- Q14:** Are hospitals part of the Inspection – Establishment Licence process?
A14: Generally the provinces have jurisdiction in hospitals, so no. Three Ontario hospitals have Drug Establishment Licences because they make radiopharmaceuticals.
- Q15:** Is this task force looking at who is required to have an inspection? We heard rumours that some won't be inspected.
A15: In terms of broad regulatory oversight and anything being done less, then only one thing is being considered and that is with respect to how often inspections are done, this could be less often. We are not going down the road of *does this type of establishment require an inspection at all?*
- Q16:** Would this project possibly lead to a reduced number of days of inspections?
A16: One part of the Good Manufacturing Practices (GMP) Review is looking at reduced number of days, but, more importantly today we will be discussing abbreviated inspections, which could mean less time with you. These options are currently on the table.
- Q17:** Have there been any decisions with respect to inspections and natural health products (NHPs)?
A17: NHPs are not part of this program. NHP consultations are coming soon.
- Q18:** What about pharmacovigilance inspections?
A18: The Good Manufacturing Practices (GMP) Review just focuses on GMP inspection; but we aren't forgetting about pharmacovigilance. We will use this for modelling for other types of inspections, like pharmacovigilance. We will identify changes that can be applied to other types of activities.

Q19: Why are some documents not posted on your website?

A19: Our information technology (IT) personnel are working on our common-look-and-feel objectives and on other backlog issues.

Q20: Do we have the resources required to do more?

A20: We have purposely not put a price tag on any options yet. We will identify resources and money needed as we identify the preferred options. In addition, we have told management that change will not work without the required support.

Q21: Will changing the inspection cycles based on risk profiles affect resources?

A21: Our management at Health Canada will be advised that if a plan cannot be backed up with the proper resources then it should not be implemented.

Q22: Will the recommendations that go to senior management be public?

A22: We will make documents accessible and public. There will be a summary report from our face-to-face consultations.

Q23: When we have the new inspection guidelines, when will they be implemented?

A23: The end goal of the Good Manufacturing Practices (GMP) Review is just to make the recommendations and our goal for this is May/June 2010. A new model would come along on a different timeline and it will be in quite some time. Before it is official there will be ample notice and good communication from Health Canada.

Q24: With respect to large-scale implementation, what's the timeframe?

A24: This depends on what is recommended.

Q25: Will we see a staged roll out?

A25: Probably, due to the number and magnitude of Drug Establishment Licence (DEL) holders.

Q26: Will the learning from these sessions transfer to other inspection programs?

A26: The learning from this program will be transferred to Medical Devices as we are responsible for Medical Devices and Drugs. However, we are not responsible for narcotic/controlled substances-related security inspections.

Appendix B – Description of proposed risk criteria

Chart 2.0 List of proposed risk criteria, with a short description, that was provided for discussion during the consultations.

Risk Factor	Explanation
Activities performed	All regulated activities that are undertaken at a particular site
Product range and complexity	The variety of products at the site and the nature of those products
Complexity and criticality of processes	Any specific, challenging technologies that the site utilizes which may result in a particular risk to Good Manufacturing Practices (GMP)
General Good Manufacturing Practices (GMP) compliance history	Pattern of significant non-compliances, lack of cooperation
Site-based recalls since last inspection	Voluntary recall of products specific to the site being inspected
Other enforcement measures/regulatory actions taken	Examples: public advisories issued, action taken on Drug Establishment Licence
Recent changes at company	Examples: changes in processes, equipment/facilities, key personnel; consider the nature of changes and if risk is increased as a result
Sole or limited source	Site is sole or limited source of supply
Concerns raised by public/other regulatory authorities	Examples: consumer complaint, rapid alerts applicable to the site
Significant concern over robustness of quality system	Consideration of the wider people/management responsibility and the ability of the site/company to maintain or improve adequate control over a period of time
Significant failures to complete actions to close previous deficiencies	Where commitments made at end of last inspection are not honoured